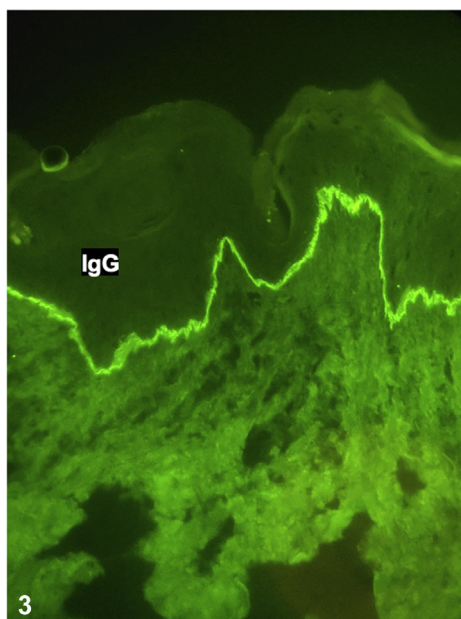
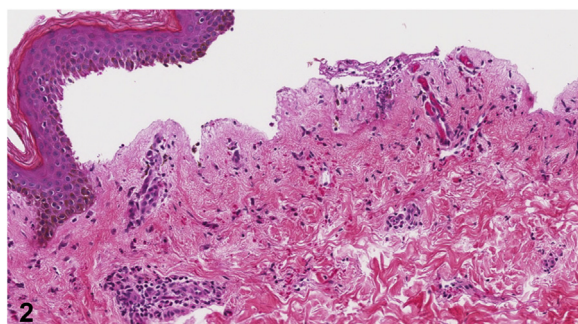


## Tense blisters in a previously healthy young woman



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**Key words:** bullous lupus; bullous systemic lupus erythematosus; subepidermal blistering; tense bullae.



A 20-year-old Black woman reported sore throat, odynophagia, cough, and skin blistering. Examination revealed tense vesicles, bullae, and well-demarcated erosions on the thighs and ulcerations on the tongue, buccal, and oropharyngeal mucosa. High-dose corticosteroids initiated at an outside hospital did not improve her condition. Antinuclear antibody, anti-double-stranded DNA, anti-Ro/SSA, and anti-La/SSB antibodies were positive. Hand swelling, joint pain, difficulty swallowing, and hemoptysis ensued. Bullae formation progressed with erosions

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involving the ears, nose, lips, extremities, and back (Fig 1). Biopsies for histology and direct immunofluorescence were performed; IgG, IgA, C3, and IgM stained the basement membrane zone (Figs 2 and 3).

**Question 1: What is the most likely diagnosis?**

- A. Bullous systemic lupus erythematosus (BSLE)
- B. Bullous pemphigoid (BP)
- C. Dermatitis herpetiformis (DH)
- D. Linear IgA bullous dermatosis (LABD)
- E. Epidermolysis bullosa acquisita (EBA)

**Answers:**

**A.** BSLE — Correct. An acute eruption of tense bullae, elevated antinuclear antibody, elevated anti-double-stranded DNA antibody, subepidermal blistering on histopathology, and immunoglobulin deposition at the basement membrane zone on direct immunofluorescence are consistent with BSLE.<sup>1</sup> Deposits of multiple immunoreactants are typically seen in BSLE, with IgG being the most common.<sup>2</sup> A neutrophil-predominant infiltrate is classically described, especially at the dermal-epidermal junction (DEJ).<sup>3</sup> The histology in this case demonstrated a pauci-inflammatory blister with neutrophils at the DEJ and focal leukocytoclasia, which is also well-described in BSLE.<sup>3</sup> In this case, a blistering eruption was the initial presentation of systemic lupus erythematosus.

**B.** BP — Incorrect. This is not supported by the patient's age, as the average age of onset for BP is between 66 and 83 years.<sup>1</sup> The absence of any medications rules out drug-induced BP, which can present at younger ages. Histopathology would show subepidermal blistering with eosinophils. The patient's serology profile supports a diagnosis of systemic lupus erythematosus and is not typical of BP.

**C.** DH — Incorrect. DH is papulovesicular, distributed on extensor surfaces, and pruritic. It is associated with the presence of antigliadin, anti-endomysium, and antitissue transglutaminase antibodies.<sup>1</sup> Subepidermal blistering with accumulation of neutrophils at the papillary tips is seen on histopathology.

**D.** LABD — Incorrect. This is unlikely, given positive serologies supportive of BSLE and multiple immunoreactants on direct immunofluorescence. Histopathology shows a subepidermal blister with a neutrophil-predominant dermal infiltrate.<sup>1</sup>

**E.** EBA — Incorrect. EBA typically occurs in middle-aged patients, while BSLE occurs

predominantly in young women with darker phototypes.<sup>3</sup> Both BSLE and EBA have anti-type VII collagen antibodies deposited in the basement membrane, but EBA does not have positive auto-antibody serologies as demonstrated in this case. Unlike BSLE, EBA commonly heals with milia and scarring<sup>1</sup> and is more refractory to treatment. Classic EBA has sparse neutrophilic inflammatory infiltrate within the dermis, while BP-like EBA has a prominent mixed infiltrate.<sup>1</sup>

**Question 2: Which immunofluorescence findings are characteristic of this condition?**

- A. Linear deposition of IgA at the DEJ with IgA binding to the epidermal side on salt-split skin
- B. Linear deposition of IgG at the DEJ with u-serration and dermal binding on salt-split skin
- C. Linear deposition of IgG at the DEJ with n-serration and dermal binding on salt-split skin
- D. Linear deposition of IgG at the DEJ with n-serration and epidermal binding on salt-split skin
- E. Granular IgA deposits in the dermal papillae and along the basement membrane zone

**Answers:**

**A.** Linear deposition of IgA at the DEJ with IgA binding to the epidermal side on salt-split skin — Incorrect. This is the finding in LABD and LABD-like EBA.<sup>1</sup>

**B.** Linear deposition of IgG at the DEJ with u-serration and dermal binding on salt-split skin — Correct. Linear IgG deposition is found in 70% to 80% of patients with BSLE.<sup>2</sup> Less frequently, granular IgG deposition may also occur.<sup>3</sup> A mixture of 3 or more immunoreactants deposited at the basement membrane zone, including IgG, IgA, IgM, and C3, is more common in BSLE compared with other autoimmune blistering diseases.<sup>2</sup> BSLE and EBA both display u-serrated pattern and dermal binding on salt-split skin but can be distinguished based on the clinical scenario and autoimmune serologies.<sup>1</sup>

**C.** Linear deposition of IgG at the DEJ with n-serration and dermal binding on salt-split skin — Incorrect. These immunofluorescence findings are found in anti-p200 and anti-LN-332 pemphigoid variants.<sup>1,2</sup>

**D.** Linear deposition of IgG at the DEJ with n-serration and epidermal binding on salt-split

skin — Incorrect. These immunofluorescence findings are found in BP.<sup>1</sup>

**E.** Granular IgA deposits in the dermal papillae and along the basement membrane zone — Incorrect. Granular IgA deposits in these locations are typical of DH.<sup>2</sup>

**Question 3: What is the treatment of choice in patients with extensive skin involvement from this condition?**

- A.** Dapsone
- B.** Prednisone
- C.** Methotrexate
- D.** Rituximab
- E.** Hydroxychloroquine

**Answers:**

**A.** Dapsone — Correct. The use of dapsone has been shown to be effective in reducing BSLE lesions in 83% to 91% of the cases.<sup>3</sup> An initial dose of 50 mg/day is common; however, escalating the dose to 100 mg/day is often required. Pretreatment glucose-6-phosphate dehydrogenase testing should be performed as severe hemolysis is a risk in glucose-6-phosphate dehydrogenase-deficient individuals.

**B.** Prednisone — Incorrect. As demonstrated in this case, BSLE lesions do not routinely resolve with systemic corticosteroid treatment alone. Corticosteroid monotherapy has an efficacy of 34%.<sup>3</sup>

**C.** Methotrexate — Incorrect. Methotrexate can be beneficial in treating subacute cutaneous lupus erythematosus, which is refractory to corticosteroids and antimalarials. There has been one report of BSLE resolution with use of methotrexate alone, but it is not first-line therapy.<sup>4</sup>

**D.** Rituximab — Incorrect. Rituximab has improved cutaneous lesions of BSLE in one case report. This is an option if dapsone cannot be tolerated or in glucose-6-phosphate dehydrogenase-deficient patients.<sup>5</sup>

**E.** Hydroxychloroquine — Incorrect. Hydroxychloroquine is commonly utilized for systemic lupus erythematosus and chronic cutaneous lupus but has not been shown to improve BSLE lesions.<sup>5</sup>

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**Abbreviations used:**

BP: bullous pemphigoid  
BSLE: bullous systemic lupus erythematosus  
DEJ: dermal-epidermal junction  
DH: dermatitis herpetiformis  
EBA: epidermolysis bullosa acquisita  
LABD: linear IgA bullous dermatosis

**Conflicts of interest**

None disclosed.

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